Exhibit 13

Transcript of audio file available at http://royalsociety.org/people/dennis-lo/

Good morning. It's our honored privilege to present in front of this distinguished audience.

Prenatal diagnosis is now an established part of modern obstetrics care. But conventional definitive methods of prenatal diagnosis like amniocentesis, shown here, are invasive and have a 1% of actually damaging or even killing the baby. And, because of this reason, over the last 40 years, many scientists around the round the world have been investigating the possibility of non-invasive prenatal diagnosis.

In 1997, my group has shown that during pregnancy, a fetus would release its DNA in the blood of the mother. So, what that means, is that open the possibility of just taking a blood sample from the mother and be able to tell something about the genetic makeup of the baby. So we now know that this DNA entering maternal circulation from the early first trimester, around seven weeks or so, at a mean fractional concentration of 10 percent and also is very clear, very quickly after delivery. So what we are detecting is really from the current baby. And this discovery has very rapidly been translated into a variety of clinical tests. For example, we can now tell the sex of the baby by detecting Y chromosome DNA in the mother's blood and this is useful for sex-linked disease like hemophilia which typically affect boys. We can also use this to tell if the blood group type of the baby is compatible with that of the mother. So these two applications are now in routine use in many parts of the world including the UK.

But, however, perhaps the number one reason why pregnant women go for prenatal testing now-a-days is because they are worried that the baby might be affected by Down syndrome, and this is caused by having an extra chromosome 21, compared with the usual two. And this is actually technically much more challenging because Down syndrome is essentially a quantitative diagnosis; we have to count the number of chromosome 21; unlike sex and blood group, which are qualitative diagnosis, where we can detect a male chromosome or detect a blood group gene. So, prior to 2007, most experts working in this area think that this technology cannot be used for the prenatal diagnosis of Down syndrome and it has actually taken us 10 years to solve this problem.

Now, the difficulty of this problem is this: now chromosome 21 is a very small chromosome, so it normally occupies about 1.3 percent of our genome. So if a baby has three copies of chromosome 21, then this number will be increased 1.5 times to 1.95 percent. But, here, we are talking about pure DNA. But, however, in the fetal DNA which has entered maternal circulation, it only occupies 10 percent of all the DNA in plasma. So, if we look at that, then the difference we're talking about is much smaller; we're talking about distinguishing 1.365 percent from 1.3 percent and this, for a DNA-based test, is extremely difficult because usually people detect DNA by a technology like PCR where you double the DNA so you can tell one copy from two, but to tell 1.3 to 1.365 is very difficult.

So in 2007, we proposed that one way to do that is to use single molecule counting, so we count single DNA molecule. And we show that the more molecules we count, the higher is the precision of the test. And we show that you need to count at least 100,000 molecules

before we can even approach this range. And, of course, at that moment, to do a test which involving 100,000 molecules is actually very tedious. But luckily over the last two or three years, with the development of next generation DNA sequencing, suddenly we have ways to actually count hundreds of millions of molecules. So, basically what we do is that we extract the DNA from the plasma of a pregnant woman and then we sequence millions of those DNA molecules. And, because we know the human genome sequence, I can use a computer to map each of those molecules back to their respective chromosomes. I can plot the proportional representation of each chromosome in plasma. And there, for every chromosome, I can calculate if there is any statistical deviation of its representation compared with a group of control. And, the method we use is a very simple statistic involving the Z score, which if there is no difference, the Z score should be around zero but if the baby has too many chromosome 21, then the Z score will shoot up. And so we have recently actually completed a very large scale study to see if this approach would work. We actually looked a total of 753 cases from Hong Kong, London, and Amsterdam, in which 86 of them has got Down syndrome. And actually the result is very encouraging. So if we can able to manage to pick up every single one of the Down syndrome baby so the sensitivity of this approach is 100 percent. And for individuals without Down syndrome babies then we actually correct 98 percent of the time. So we have a specificity of 98 percent. That means if you use this technology you can actually reduce the probability of amniocentesis by 98 percent. So we actually published this data in January of this year. And just a few weeks later, a group based in USA have also done a similar result with 450 cases with very similar sensitive and specificity. So, basically, I think that the non-invasive prenatal testing Down syndrome is essentially solved.

So what that means from those two publications is as long as we count 10 million molecules per case, we can have a close to perfect test. And that is important and actually practical because with the latest generation of sequencer, like the one shown here, in which every time you switch on the machine you can analyze one billion molecules, that means that every time you use the machine, I can share the one billion molecules with 100 plasma samples because each one I need 10 million. So it means that if you run this machine one time a week, so every year I can analyze 5,000 samples per machine, despite the fact the machine is very expensive. And this is already very practical. For example, like a city like Hong Kong where with 7 million people, every year we have 3,000 high-risk pregnancies which currently will be investigated by amniocentesis. So what we are proposing now is to actually do the sequencing test for those 3,000 women. And, for that, one machine is enough for whole of Hong Kong.

So, basically, now, the non-invasive prenatal testing of Down syndrome is essentially solved. What's left now is really the practical aspect of trying to get into clinical practice.

The next question is how far can we actually push this technology? For example, is it possible to scan the entire fetal genome using this approach? Now we been thinking about this alongside Down syndrome project, and our conclusion at that time is actually very difficult. The reason is because the genome is fragmented into millions of pieces in the plasma. And also the fetal DNA is surrounded by sea of maternal DNA, so no way to try to assemble fetal genome this way. It's like to assemble a jigsaw puzzle with a million of pieces. And, also, before you start with that jigsaw, you mix in ten times of another jigsaw and then you start with the first one. So initially we thought it might just be too difficult

until one day I went to see this film with my wife and you may recall the first 10 minutes of the film is in IMAX 3D. So I put on the 3D goggles and I saw the Harry Potter sign flying towards me. And when I saw the H with this two lines, suddenly I have an inspiration. And I thought back to the fetal genome has got two halves; one half is inherited from the father and the other half is inherited from the mother. And of two halves actually require different treatment. Like for example, like this picture is the father's genome and this one is the mother's genome; so baby will have one-half from father and the other half from the mother. So, now in the mother's blood, there is a lot of the mother's genome floating around and we're trying to hunt for the fetal genome. Now for the first half, which is the father's half, what we do is we compare the father and mother's genome and try to find things which is only present in the father's genome and which is easy to find, like the flower. And then we go into the mother's blood and hunt for the flower. So provided that we have enough of that flower, you solve the first half of the problem; you got a paternal genome. Now for the maternal genome it's a bit more difficult because the fetal genome is surrounded by this sea of maternal genome in the mother's blood. So, by definition, anything which the baby has inherited from the mother, the mother will have it herself. So you cannot use a qualitative approach. You have to use something quantitative. So what I mean is this: In the mother's genome, the left-hand half and the right-hand half of her genome should be present in a ratio of 1 to 1. So now imagine if mother gives the right-hand half to her baby and the baby releases back into the mother's blood; then theoretically inside the mother's blood there should be a little bit excess of the right-hand half compared with the left-hand half. So basically what we do is then go into mother's blood and we count the number of halves, and the half which is in excess is the half inherited by the baby. But of course to do this with two halves is one thing; to do it for millions of pieces is another. To assemble is a third one. But, of course, at least we have the theory that this can be done. So, the question is, does it work.

To see if it works, we study a couple which were referred to a hospital for prenatal diagnosis of beta thalassemia, which is a genetic form of anemia. So the father carry a mutation which involving deletion of four base pair in the gene and the mother carries a point mutation and the mother is 12 weeks pregnant and we took the blood from her and then sequence her blood. Now to show you how difficult this project is. Now for Down syndrome test, all I have to do is sequence 10 million molecules and you have a close to perfect test. But for this project I have to sequence 4 billion molecules which is like sequencing a genome 65 times; and in the end this is the result. So the chromosomes are plotted like this, under a circle, and the blue one is the fetal specific reads, and the red one is a total read which is mainly from the mother. So you see at a glance that basically the entire genome is there in the plasma and the mom and baby's sequence is seem to have a constant relationship with each other, they go up and down. That means the fractional concentration of fetal genome is constant throughout the whole genome and indeed in this case, it is at 11.5 percent.

So now having the whole genome in our computer we can then scan it for literally any prenatal diagnosis that we want to do. Like for example in the case of beta thalassemia the gene is on chromosome 11. So we can home in to that region. So this is a gene which is involved that is the father's mutation and that's the mother's mutation. So the father's mutation, in this case, is a four base pair deletion. So this is like the flower I showed you just now. So then we go in and scan the computer sequence and find it and there are 11

instances where we can see his four-base pair deletion. So, in other words, the baby has inherited the father's mutation.

So how about the mother's mutation? So this time we have to use this counting approach. So normally in the mother's genome, the normal and mutant copy of a gene is present at the ratio of 1 to 1. So, imagine if the mother had passed the mutant copy to the baby and baby has released it back into the mother's blood then there should be an excess of mutant compared to normal in the mother's blood. But if you do the statistics, in order to have this in your statistical significance we need to cover this four thousand times and that means sequencing a genome four thousand times and that would make the project prohibitively expensive. So we need to do something more cost effective. So instead of just focusing on the mutation itself we also looked at a whole series of genetic markers which are linked, which are on the same chromosome as the mutant and normal copy. So, in other words, we're looking at a whole haplotype together. And then we ask the question, which of these two haplotypes—the normal one or the mutant one—which is in excess in the mother's blood? And we call this relative haplotype dosage, riddle [phonetic] analysis. So when this haplotype is released in the mother's blood, the DNA got fragmented into millions of pieces so when we do the sequencing then we map each of those back in the haplotype. So in this case we show that it's a normal haplotype which is in excess. So in other words the baby has inherited the normal gene from mother but the abnormal gene from the father, so the baby is just a carrier. So this work was actually published and was chosen on the cover of this magazine a few months ago. And so we show for the first time we can scan the entire fetal genome using a maternal blood sample. But the problem with it at the moment is it's very expensive. It actually cost us two hundred thousand US dollars to do this single case. And then of course you ask me why do you bother? The reason is because somebody need to do it at least once to show that the entire fetal genome is there. After you know it's present, then I think the future practical application of that is to us a targeted version of that in which you target a specific genetic disease which are common in that population and just do it then. I think with that you can probably reduce the cost to maybe one or two thousand US.

So, in conclusion, hope I have shown you that over the last 14 years or so would have shown a fetal DNA in maternal plasma can be used as a tool for non-invasive prenatal diagnosis and a lot of the recent development focus on the sequencing approach and with this the prenatal detection of Down syndrome is already solved and would have also shown you the principle of doing a fetal genome scanning. In the future what we will involve is trying to make this approach more practical and of course a lot of social and ethical implications which will need to be discussed.

So, finally, I'd like to thank my group members for generating the data which I present to you today and my various local and international collaborators. So thank you very much.